REMARKS

Claims 1-18 are pending in the present application. Claims 9-11 and 18 have been withdrawn. Claims 19-23 have been added. Claim 1 has been amended. Therefore, claims 1-8, 12-17 and 19-23 will be pending upon entry of the present amendment.

Claim 1 was amended to correct a grammatical error. Suport for new claims 19-21 can be found, for example, at least in the claims as originally filed and on page 4, lines 2-9 and 24. Support for new claims 22 and 23 can be found, for example, at least in the claim 14 as originally filed and at page 30, lines 2-16. No new matter has been added.

Applicants note that some of the references cited on the Information Disclosure - statement filed on November 8, 2004, had not been considered by the Examiner, because the Examiner was not able to locate the references in the parent file. However, based on a conversation between the Examiner and Applicants' attorney on August 7, 2006, the references have subsequently been located and will be considered.

Rejection of Claims 1-8, 12, 13, and 15-17 under 35 U.S.C. § 103(a)

Claims 1-8, 12, 13, and 15-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ericinska *et al., Journal of Cerebral Blood Flow and Metabolism*, 9:2-19 (1989); in view of Beal *et al., Journal of Neurochemistry* 57(3):1068-1073 (1991), in view of Roberts *et al., American Journal of Physiology* 243(6):H911-H916 (1982). Applicants respectfully traverse.

Claim 1 and its dependent claims are directed to a method of treating a nervous system disease by administering an amount of creatine, creatine phosphate or a creatine analog or a salt thereof, sufficient to prevent, reduce, ameliorate or eliminate the disease. Claim 4 and its dependent claims are directed to a method of treating a nervous system disease by administering an amount of a creatine compound of a general formula given above, sufficient to prevent, reduce, ameliorate or eliminate the disease. Claim 17 is directed to a method for alleviating in a subject being treated for a nervous system disease toxic side effects of drugs used to treat the nervous system disease.

The primary reference, Ericinska *et al.*, is a general reference which states that the creatine phosphate/creatine system ("PCr/Cr") system is a high energy reservoir present in the central nervous system. Ericinska *et al.* notes that the PCr/Cr system is linked to the adenine nucleotides through a rapid equilibration in the creatine phosphokinase reaction.

Applicants note that the primary reference neither teaches nor suggests methods for treating a nervous system disease, let alone a method for treating a nervous system

disease using a creatine compound. Furthermore, Applicants also note that this reference fails to teach or suggest any methods for alleviating the toxic side effects of drugs used to treat diseases of the nervous system.

Beal *et al.*, a secondary reference, is about the discovery that aminooxyacetic acid (AOAA) causes excitotoxic lesions, which are similar to those found in Huntington's disease patients. Beal *et al.* states that the excitotoxic legions may be the result of an impairment of the intracellular energy mechanism. In particular, Beal *et al.* notes that "AOAA is a potent inhibitor of aspartate transaminase, which is an essential component of the maleate-aspartate shunt across mitochondrial membranes...Inhibition of aspartate aminotransferase in both brain slices and synaptosomes results in decreased oxygen consumption, decreased glucose and pyruvate oxidation, a decrease in ATP/ADP ratios, and an increase of the NADH/NAD ratio in the cytosol. Interstitial injections of AOAA resulted in fourfold significant increase in stritial lactate levels and significant decreases in ATP concentrations."

Beal *et al.* fails to overcome the deficiencies of the primary reference. Although the Examiner relies on Beal *et al.* to establish that connection between ATP levels and Huntington's disease, Beal *et al.* does not teach that modulation of ATP levels would reverse the effects of treatment with AOAA and/or Huntington's disease. Rather, Beal *et al.* shows that there are many downstream effects of blocking the aspartate transaminase enzyme, including elevated lactate levels and a decrease in ATP concentrations. Beal *et al.* fails to suggest that the legions could be treated by solely increasing the ATP concentrations without additional treatments to decrease the levels of lactate in the cells. Beal *et al.* fails to overcome the deficiencies of the primary reference and fails to teach or suggest that Huntington's disease is caused by a deficiency of ATP. Rather, Beal *et al.* teaches that excitotoxic legions can be formed by treatment of tissue with AOAA.

Roberts *et al.*, a secondary reference, is directed to treating rats with ischemia a creatine analogue. Roberts *et al.* notes that while cyclocreatine significantly increased the time to half-maximal rigor, creatine actually decreased the time to half maximal-rigor as compared to the rats fed the control chow. Therefore, Roberts *et al.* does not provide "motivation to treat disorders via the administration of creatine and/or creatine phosphate because of successful treatment illustrated by Roberts." Furthermore, Roberts *et al.* does not teach or suggest administration of creatine compounds to humans, only rats.

Roberts *et al.* fails to overcome the deficiencies of Ericinska *et al.* and Beal *et al.*, alone or in combination. Rather, an ordinarily skilled artisan would not be able to use Roberts *et al.* to establish that the administration of creatine compounds would raise intracellular ATP levels, since the experiments on rats gave mixed results and certainly

did not show successful treatment using creatine, as suggested by the Examiner. Furthermore, Applicants also note that none of the references teach or suggest any methods for alleviating the toxic side effects of drugs used to treat diseases of the nervous system, let alone by the administration of a creatine compound.

Therefore, Applicants respectfully request that this rejection of claims 1-8, 12, 13, and 15-17 under 35 U.S.C. § 103(a), be withdrawn.

Rejection of Claim 14 under 35 U.S.C. § 103(a)

Claim 14 is rejected as being unpatentable over Ericinska *et al.*, Beal *et al.*, Roberts *et al.*, in view of Nuti *et al. Riv. Neur.* 61(6):225-7 (1991). Applicants respectfully traverse this rejection.

Claim 14 is directed to a method for treating a nervous system disease, by administering to a subject an effective amount of a creatine compound and a neurotransmitter, a neurotransmitter analog, a steroid, an immunomodulating agent, or an immune suppressive agent.

Ericinska *et al.*, Beal *et al.*, and Roberts *et al.* have been described above. Nuti *et al.* is directed to a method for treating Huntington's chorea using dexamethasone.

As noted above, Ericinska *et al.*, Beal *et al.*, and Roberts *et al.*. fail to teach or suggest a method of treating a nervous disease by the administration of a creatine compound. Nuti *et al.* fails to overcome this deficiency. Although Nuti *et al.* describes the use of dexamethasone as a potential Huntington's chorea therapy, it does not teach or suggest methods of treating nervous system diseases using creatine in combination with a neurotransmitter, a neurotransmitter analog, a steroid, an immunomodulating agent, or an immune suppressive agent, as claimed by Applicants.

Therefore, Applicants respectfully request that this rejection of claim 14, under 35 U.S.C. § 103(a) be withdrawn.

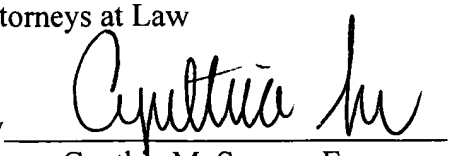
SUMMARY

Amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The amendments made to the claims are not related to any issues of patentability.

In view of the remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the Elizabeth A. Hanley, Esq. at (617) 227-7400.

Date: August 8, 2006

LAHIVE & COCKFIELD, LLP
Attorneys at Law

By 

Cynthia M. Soroos, Esq.
Reg. No. 53,623
28 State Street
Boston, MA 02109
(617) 227-7400
(617) 742-4214